

## SEQUENCE LISTING

<110> ALDAZ, MARCELO C. BEDNAREK, ANDRZEJ <120> WWOX: A PUTATIVE TUMOR SUPPRESSOR GENE MUTATED IN MULTIPLE CANCERS <130> UTSC:671US <140> 09/978,318 <141> 2001-10-15 <150> 60/240,277 <151> 2000-10-13 <160> 68 <170> PatentIn Ver. 2.1 <210> 1 <211> 2264 <212> DNA <213> Human <400> 1 gcagtgcgca ggcgtgagcg gtcgggcccc gacgcgcgcg ggtctcgttt ggagcgggag 60 tgagttcctg agcgagtgga cccggcagcg ggcgataggg gggccaggtg cctccacagt 120 cagccatggc agcgctgcgc tacgcggggc tggacgacac ggacagtgag gacgagctgc 180 ctccgggctg ggaggagaga accaccaagg acggctgggt ttactacgcc aatcacaccg 240 aggagaagac tcagtgggaa catccaaaaa ctggaaaaag aaaacgagtg gcaggagatt 300 tgccatacgg atgggaacaa gaaactgatg agaacggaca agtgtttttt gttgaccata 360 taaataaaag aaccacctac ttggacccaa gactggcgtt tactgtggat gataatccga 420 ccaagccaac cacceggcaa agatacgaeg gcagcaccac tgccatggaa attetecagg 480 gccgggattt cactggcaaa gtggttgtgg tcactggagc taattcagga atagggttcg 540 aaaccgccaa gtcttttgcc ctccatggtg cacatgtgat cttggcctgc aggaacatgg 600 caagggcgag tgaagcagtg tcacgcattt tagaagaatg gcataaagcc aaggtagaag 660 caatgaccct ggacctcgct ctgctccgta gcgtgcagca ttttgctgaa gcattcaagg 720 ccaagaatgt gcctcttcat gtgcttgtgt gcaacgcagc aacttttgct ctaccctgga 780 gtctcaccaa agatggcctg gagaccacct ttcaagtgaa tcatctgggg cacttctacc 840 ttgtccaget cetecaggat gttttgtgcc getcagetee tgcccgtgte attgtggtet 900 cctcaqaqtc ccatcqattt acaqatatta acqactcctt qqqaaaactq qacttcaqtc 960 geetetetee aacaaaaaa gaetattggg egatgetgge ttataacagg tecaagetet 1020 gcaacatcct cttctccaac gagetgcacc gtcgcctctc cccacgcggg gtcacgtcga 1080 acgcagtgca tcctggaaat atgatgtact ccaacattca tcgcagctgg tgggtgtaca 1140 cactgctgtt taccttggcg aggcctttca ccaagtccat gcaacaggga gctgccacca 1200 ccgtgtactg tgctgctgtc ccagaactgg agggtctggg agggatgtac ttcaacaact 1260 gctgccqctg catqccctca ccaqaaqctc aqagcqaaga qacqqcccqq accctqtgqg 1320 cgctcagcga gaggctgatc caagaacggc ttggcagcca gtccggctaa gtggagctca 1380 gageggatgg geacacacac cegecetgtg tgtgteeeet caegeaagtg ceagggetgg 1440 gccccttcca aatgtccctc caacacagat ccgcaagagt aaaggaaata agagcagtca 1500 caacagagtg aaaaatctta agtaccaatg ggaagcaggg aattcctggg gtaaagtatc 1560

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Thr Gly Lys Arg Lys Arg Val Ala Gly Asp Leu Pro Tyr Gly Trp Glu 50 55 60

Gln Glu Thr Asp Glu Asn Gly Gln Val Phe Phe Val Asp His Ile Asn 65 70 75 80

Lys Arg Thr Thr Tyr Leu Asp Pro Arg Leu Ala Phe Thr Val Asp Asp 85 90 95

Asn Pro Thr Lys Pro Thr Thr Arg Gln Arg Tyr Asp Gly Ser Thr Thr
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Val Thr Gly Ala Asn Ser Gly Ile Gly Phe Glu Thr Ala Lys Ser Phe 130 135 140

Ala Leu His Gly Ala His Val Ile Leu Ala Cys Arg Asn Met Ala Arg 145 150 155 160

Ala Ser Glu Ala Val Ser Arg Ile Leu Glu Glu Trp His Lys Ala Lys 165 170 175

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Phe Ala Glu Ala Phe Lys Ala Lys Asn Val Pro Leu His Val Leu Val
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Cys Asn Ala Ala Thr Phe Ala Leu Pro Trp Ser Leu Thr Lys Asp Gly 210 215 220

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| Gln         | Leu                             | Leu        | Gln        | Asp<br>245 | Val        | Leu        | Cys        | Arg        | Ser<br>250 | Ala        | Pro        | Ala        | Arg        | Val<br>255 | Ile        |    |
| Val         | Val                             | Ser        | Ser<br>260 | Glu        | Ser        | His        | Arg        | Phe<br>265 | Thr        | Asp        | Ile        | Asn        | Asp<br>270 | Ser        | Leu        |    |
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| Ala         | Met<br>290                      | Leu        | Ala        | Tyr        | Asn        | Arg<br>295 | Ser        | Lys        | Leu        | Cys        | Asn<br>300 | Ile        | Leu        | Phe        | Ser        |    |
| Asn<br>305  | Glu                             | Leu        | His        | Arg        | Arg<br>310 | Leu        | Ser        | Pro        | Arg        | Gly<br>315 | Val        | Thr        | Ser        | Asn        | Ala<br>320 |    |
| Val         | His                             | Pro        | Gly        | Asn<br>325 | Met        | Met        | Tyr        | Ser        | Asn<br>330 | Ile        | His        | Arg        | Ser        | Trp<br>335 | Trp        |    |
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| Gln         | Gln                             | Gly<br>355 | Ala        | Ala        | Thr        | Thr        | Val<br>360 | Tyr        | Cys        | Ala        | Ala        | Val<br>365 | Pro        | Glu        | Leu        |    |
| Glu         | Gly<br>370                      | Leu        | Gly        | Gly        | Met        | Tyr<br>375 | Phe        | Asn        | Asn        | Cys        | Cys<br>380 | Arg        | Cys        | Met        | Pro        |    |
| Ser<br>385  | Pro                             | Glu        | Ala        | Gln        | Ser<br>390 | Glu        | Glu        | Thr        | Ala        | Arg<br>395 | Thr        | Leu        | Trp        | Ala        | Leu<br>400 |    |
| Ser         | Glu                             | Arg        | Leu        | Ile<br>405 | Gln        | Glu        | Arg        | Leu        | Gly<br>410 | Ser        | Gln        | Ser        | Gly        |            |            |    |
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|---|-------------------|---|---|---|---|---|---|---|-----|---|---|---|---|---|---|-----|
|   | ggc<br>Gly<br>30  |   |   |   |   |   |   |   |     |   |   |   |   |   |   | 265 |
| _ | cat<br>His        |   |   |   |   |   | _ |   | _   |   | _ |   | _ | _ |   | 313 |
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|   | agc<br>Ser<br>110 |   |   | _ | _ | _ |   |   | . – |   |   | _ |   |   |   | 505 |
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|   | gat<br>Asp        |   |   |   |   |   |   |   |     |   |   |   |   |   |   | 649 |
|   | gag<br>Glu        | _ | _ | _ |   | _ | _ |   |     |   | _ | _ | _ |   | _ | 697 |
| _ | cca<br>Pro<br>190 | _ | _ | _ |   | _ |   | _ |     |   | _ |   | _ | _ | _ | 745 |
|   | tgg<br>Trp        |   |   |   |   |   |   |   |     |   |   |   |   |   |   | 793 |
|   | gct<br>Ala        |   |   |   |   |   |   |   |     |   |   |   |   |   |   | 841 |

225 230 235

| aaa gga aat aag agc agt cac aac aga gtg aaa aat ctt aag tac caa<br>Lys Gly Asn Lys Ser Ser His Asn Arg Val Lys Asn Leu Lys Tyr Gln<br>240 245 250 | 389  |
|---|------|
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| gct agg cat agg tct ctt tgc ttt ctg gtg gtg gcc tgt ttg aaa gta Ala Arg His Arg Ser Leu Cys Phe Leu Val Val Ala Cys Leu Lys Val 270 275 280       | 985  |
| aaa acc tgc ttg gtg tgt agg ttc cgt atc tcc ctg gag aag cac cag Lys Thr Cys Leu Val Cys Arg Phe Arg Ile Ser Leu Glu Lys His Gln 285 290 295 300   | 1033 |
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Asn Pro Thr Lys Pro Thr Thr Arg Gln Arg Tyr Asp Gly Ser Thr Thr
                                105
Ala Met Glu Ile Leu Gln Gly Arg Asp Phe Thr Gly Lys Val Val Val
                            120
Val Thr Gly Ala Asn Ser Gly Ile Ala Thr Gly Ser Cys His His Arg
                        135
                                            140
Val Leu Cys Cys Cys Pro Arg Thr Gly Gly Ser Gly Arg Asp Val Leu
                    150
                                        155
Gln Gln Leu Leu Pro Leu His Ala Leu Thr Arg Ser Ser Glu Arg Arg
                                    170
Asp Gly Pro Asp Pro Val Gly Ala Gln Arg Glu Ala Asp Pro Arg Thr
                                185
Ala Trp Gln Pro Val Arg Leu Ser Gly Ala Gln Ser Gly Trp Ala His
                            200
                                                205
Thr Pro Ala Leu Cys Val Ser Pro His Ala Ser Ala Arg Ala Gly Pro
                        215
                                            220
Leu Pro Asn Val Pro Pro Thr Gln Ile Arg Lys Ser Lys Gly Asn Lys
                    230
                                        235
Ser Ser His Asn Arg Val Lys Asn Leu Lys Tyr Gln Trp Glu Ala Gly
               245
                                    250
Asn Ser Trp Gly Lys Val Ser Leu Phe Trp Gly Trp Ala Arg His Arg
            260
                                265
Ser Leu Cys Phe Leu Val Val Ala Cys Leu Lys Val Lys Thr Cys Leu
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Val Cys Arg Phe Arg Ile Ser Leu Glu Lys His Gln Gln Phe Ser Phe
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Phe Tyr Cys Tyr Arg Ile Ala
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tecacagtea gee atg gea geg etg ege tae geg ggg etg gae gae aeg
                                                                   169
               Met Ala Ala Leu Arg Tyr Ala Gly Leu Asp Asp Thr
                                                                   217
gac agt gag gac gag ctg cct ccg ggc tgg gag gag aga acc acc aag
Asp Ser Glu Asp Glu Leu Pro Pro Gly Trp Glu Glu Arg Thr Thr Lys
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Gln Glu Thr Asp Glu Asn Gly Gln Val Phe Phe Val Asp His Ile Asn

75

70

| _   |      |       | _    |      |       | -     |       |       |       |      |            | _     |       | cag<br>Gln        |        | 265  |
|-----|------|-------|------|------|-------|-------|-------|-------|-------|------|------------|-------|-------|-------------------|--------|------|
| -   |      |       |      |      |       |       | _     |       |       |      | _          |       | _     | ttg<br>Leu        |        | 313  |
|     |      |       | -    |      | _     |       | _     |       |       |      |            | -     |       | ttt<br>Phe<br>75  | _      | 361  |
| _   |      |       |      |      | _     |       |       |       | _     |      |            |       | _     | gcg<br>Ala        |        | 409  |
|     |      | _     | _    |      | _     |       | _     |       |       |      |            |       | _     | tac<br>Tyr        | _      | 457  |
|     | _    |       |      | _    | _     | _     |       |       | _     |      |            | -     |       | act<br>Thr        |        | 505  |
|     |      | _     |      | _    |       |       | _     |       |       |      |            |       |       | gaa<br>Glu        |        | 553  |
| _   | _    |       |      | -    |       |       |       | _     |       |      |            | _     | _     | tgc<br>Cys<br>155 |        | 601  |
|     |      |       |      |      |       |       |       |       |       |      |            |       |       | gaa<br>Glu        |        | 649  |
|     | _    |       | _    | _    |       |       |       |       | _     | _    | _          | _     |       | gaa<br>Glu        | _      | 697  |
|     |      | _     |      |      | _     |       |       |       |       | _    | _          | -     | _     | atg<br>Met        |        | 745  |
|     |      | _     | _    | -    | _     | _     |       | _     | _     |      |            | -     |       | gcg<br>Ala        |        | 793  |
|     |      |       |      |      |       |       |       |       |       |      | cag<br>Gln |       |       | taa<br>235        |        | 838  |
| gtg | gagc | tca 🤅 | gagc | ggat | aa a  | caca  | cacao | c cc  | gecet | tgtg | tgt        | gtcc  | cct ( | cacgo             | caagtg | 898  |
| cca | gggc | tgg ( | gccc | cttc | ca a  | atgto | ccct  | c caa | acaca | agat | ccg        | caaga | agt a | aaagg             | gaaata | 958  |
| aga | gcag | tca ( | caac | agag | tg aa | aaaat | tctta | a agt | cacca | aatg | ggaa       | agca  | ggg ( | aatto             | ectggg | 1018 |

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<211> 234

<212> PRT

<213> Homo sapiens

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Met Ala Ala Leu Arg Tyr Ala Gly Leu Asp Asp Thr Asp Ser Glu Asp Glu Leu Pro Pro Gly Trp Glu Glu Arg Thr Thr Lys Asp Gly Trp Val 25 Tyr Tyr Ala Asn His Thr Glu Glu Lys Thr Gln Trp Glu His Pro Lys Thr Gly Lys Arg Lys Arg Val Ala Gly Asp Leu Pro Tyr Gly Trp Glu 55 Gln Glu Thr Asp Glu Asn Gly Gln Val Phe Phe Val Asp His Ile Asn 70 75 Lys Arg Thr Thr Tyr Leu Asp Pro Arg Leu Ala Phe Thr Val Asp Asp 85 90 Asn Pro Thr Lys Pro Thr Thr Arg Gln Arg Tyr Asp Gly Ser Thr Thr 105 Ala Met Glu Ile Leu Gln Gly Arg Asp Phe Thr Gly Lys Val Val Val 120 125 Val Thr Gly Ala Asn Ser Gly Ile Gly Phe Glu Thr Ala Lys Ser Phe 135 140 Ala Leu His Gly Ala His Val Ile Leu Ala Cys Arg Asn Met Ala Arg 150 155 Ala Ser Glu Ala Val Ser Arg Ile Leu Glu Glu Trp Gln Gln Gly Ala 170 165 Ala Thr Thr Val Tyr Cys Ala Ala Val Pro Glu Leu Glu Gly Leu Gly Gly Met Tyr Phe Asn Asn Cys Cys Arg Cys Met Pro Ser Pro Glu Ala

|              |                | 195   |       |       |            |            | 200        |     |     |     |            | 205 |     |     |     |     |
|--------------|----------------|-------|-------|-------|------------|------------|------------|-----|-----|-----|------------|-----|-----|-----|-----|-----|
| Gln          | Ser<br>210     | Glu   | Glu   | Thr   | Ala        | Arg<br>215 | Thr        | Leu | Trp | Ala | Leu<br>220 | Ser | Glu | Arg | Leu |     |
| Ile<br>225   |                |       | Arg   | Leu   | Gly<br>230 |            | Gln        | Ser | Gly |     |            |     |     |     |     |     |
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| <213         |                |       |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
|              |                |       | sapie | ens   |            |            |            |     |     |     |            |     |     |     |     |     |
| < 400        |                |       |       |       | _          |            |            |     |     |     |            |     |     |     |     | 1.0 |
| agca         | agge           | grg a | agcgg | gregg | 3          |            |            |     |     |     |            |     |     |     |     | 19  |
| <210         | 0> 3           | 5     |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
| <212         |                |       |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
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| <400         |                |       |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
| acto         | ggat           | ttc a | agctt | tcgt  | gg to      | cg         |            |     |     |     | a.         |     |     |     |     | 23  |
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| <400         | 0 > 3          | 6     |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
| tcc          | gtgg           | gct ( | gtgca | agggt | tc         |            |            |     |     |     |            |     |     |     |     | 20  |
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|              |                |       | ttcct | ttct  | ta ta      | atct       | ggc        |     |     |     |            |     |     |     |     | 28  |
| 0.7          |                | •     |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
| <210<br><210 | J> 3<br>1> 2   |       |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
|              | 2 > D          |       |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
| <21          | 3> H           | omo   | sapie | ens   |            |            |            |     |     |     |            |     |     |     |     |     |
| <40          |                |       | a     | a+ a+ | ~a +.      | at a a i   | <b>-</b> a |     |     |     |            |     |     |     |     | 27  |
| acc          | Julia          |       | cacco | ccac  | ga L       | cca        |            |     |     |     |            |     |     |     |     | 21  |
| <21          | 0 > 3          | 9     |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
|              | 1> 2           |       |       |       |            |            |            |     |     |     |            |     |     |     |     |     |
|              | 2 > D<br>3 > H |       | sapi  | ens   |            |            |            |     |     |     |            |     |     |     |     |     |

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| egetetetetg | gcacctacga gaag | 47         |
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